Refine Search

Search Results -

Terms	Documents
L3 and (424/450).ccls.	57

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L4

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Monday, March 19, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L4	L3 and 424/450.ccls.	57	L4
L3	L2 and (ammonium adj1 sulfate)	443	L3
L2	liposome same lyophiliz$	3499	L2
L1	liposome same lyophiliz$ same (ammonium adj1 sulfate)	6	L1

END OF SEARCH HISTORY

L4: Entry 33 of 57 File: USPT Jul 30, 2002

DOCUMENT-IDENTIFIER: US 6426086 B1
TITLE: pH-sensitive, serum-stable liposomes

Detailed Description Text (58):
Suitable methods include, e.g., sonication, extrusion, high pressure/homogenization, microfluidization, detergent dialysis, calcium-induced fusion of small liposome vesicles, and ether-infusion methods, all well known in the art. One method produces multilamellar vesicles of heterogeneous sizes. In this method, the vesicle-forming lipids are dissolved in a suitable organic solvent or solvent system and dried under vacuum or an inert gas to form a thin lipid film. If desired, the film may be redissolved in a suitable solvent, such as tertiary butanol, and then lyophilized to form a more homogeneous lipid mixture which is in a more easily hydrated powder-like form. This film is covered with an aqueous buffered solution and allowed to hydrate, typically over a 15-60 minute period with agitation. The size distribution of the resulting multilamellar vesicles can be shifted toward smaller sizes by hydrating the lipids under more vigorous agitation conditions or by adding solubilizing detergents such as deoxycholate. In a preferred embodiment, multilamellar liposomes are produced by the reverse phase evaporation method of Szoka & Papahadjopoulos, Proc. Natl. Acad. Sci. USA, 75: 4194-4198 (1978).

Detailed Description Text (82):
The resulting aqueous solutions may be packaged for use or filtered under aseptic conditions and lyophilized, the lyophilized preparation being combined with a sterile aqueous solution prior to administration. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH adjusting and buffering agents, tonicity adjusting agents and the like, including, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, and calcium chloride. Additionally, the liposome suspension may include lipid-protective agents which protect lipids against free-radical and lipid-peroxidative damages on storage. Lipophilic free-radical quenchers, such as alphatocopherol and water-soluble iron-specific chelators, such as ferrioxamine, are suitable.

Detailed Description Text (84):
Preferably, the pharmaceutical compositions are administered parenterally, i.e., intraarticularly, intravenously, intraperitoneally, subcutaneously, or intramuscularly. More preferably, the pharmaceutical compositions are administered intravenously or intraperitoneally by a bolus injection. Particular formulations which are suitable for this use are found in Remington's Pharmaceutical Sciences, Mack Publishing Company, Philadelphia, Pa., 17th ed. (1985) and 18.sup.th Ed. (1990). Typically, the formulations will comprise a solution of the liposomes suspended in an acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers may be used, e.g., water, buffered water, 0.9% isotonic saline, and the like. These compositions may be sterilized by conventional, well known sterilization techniques, or may be sterile filtered. The resulting aqueous solutions may be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous solution prior to administration. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH adjusting and

buffering agents, tonicity adjusting agents, wetting agents and the like, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, calcium chloride, sorbitan monolaurate, triethanolamine oleate, etc.

Detailed Description Text (123):
Liposomes were prepared by a combination of six cycles of rapid freeze-thaw, alternatively placing the lipid suspension in dry ice/ethanol and then a 60.degree. C. water bath, and then extrusion through 100 nm and 50 nm filters. HPTS was encapsulated in liposomes by including it and DPX (a water soluble fluorescence quencher) at concentrations of 35 mM HPTS and 50 mM DPX in the hydrating solution (pH 8.0). Doxorubicin was encapsulated in liposomes using an ammonium sulfate remote-loading technique as described previously (Haran et al., Biochim. Biophys. Acta 151:201-215 (1993); Lasic et al., FEBS Lett. 312:255-258 (1992)). Briefly, liposomes were hydrated in 250 mM ammonium sulfate (pH 5.5) and extruded through 100 and 50 nm filters. The extruded liposomes were then separated from unencapsulated ammonium sulfate on a Sephadex G-75 size-exclusion column and collected in a 15 ml cell culture tube containing the dry drug. Doxorubicin was added at a concentration of 1.5 mg of doxorubicin (9 mg of total powder since it also contains lactose monohydrate at a ratio of 1:6 w/w). After briefly vortexing to make sure all the drug was in solution, the liposomes were incubated for 1 h at 55.degree. C. in a hot water bath to finish the loading process. The liposomes were then separated from any free doxorubicin on a size-exclusion column.

Current US Original Classification (1):
424/450

Previous Doc Next Doc Go to Doc#

Refine Search

Search Results -

Terms	Documents
liposome same doxorubicin same (ammonium adj1 sulfate)	43

Database: US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L1

Refine Search

Recall Text Clear Interrupt

Search History

DATE: Monday, March 19, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L1	liposome same doxorubicin same (ammonium adj1 sulfate)	43	L1

END OF SEARCH HISTORY

L1: Entry 36 of 43 File: USPT May 31, 1994

DOCUMENT-IDENTIFIER: US 5316771 A
TITLE: Method of amphiphatic drug loading in liposomes by ammonium ion gradient

Detailed Description Text (36):
Doxorubicin is an amphiphatic drug similar, in some of its physical properties, to acridine orange. It is a weak amphiphatic base having the amino group (pK=8.25). Therefore, the drug has properties similar to acridine orange allowing the pH gradient created between the inside and outside of the liposomes to cause doxorubicin's loading into the internal aqueous compartment of the liposomes. For the purpose of loading the drug, the ammonium sulfate liposomes formed according to Examples 1-3, were passed on a Sephadex G-50 column preequilibrated sodium chloride solution, to generate pH gradient, and added to the doxorubicin solution in saline-desferal according to methods in Examples 1C-3C. The kinetics of incorporation of the drug is described in FIG. 3. Two preparations of liposomes were used, one composed of EPC and cholesterol in molar ratio of 2:1; and second of DPPC and cholesterol in molar ratio 2:1.

Detailed Description Text (37):
FIG. 3 shows the kinetics of the loading of doxorubicin into ammonium sulfate liposomes. The loading was started after removal of external untrapped ammonium sulfate by Sephadex G-50 gel exclusion chromatography. Doxorubicin was incubated for the indicated time with either EPC/cholesterol (-.-.-.-) liposomes at 25.degree. C. or DPPC/cholesterol liposomes (- - - -) at 50.degree. C. At the end of incubation period, unincorporated doxorubicin was removed by adsorption on a Dowex 50W column and the concentration of the phospholipid and drug were determined and used to calculate the Doxorubicin/Lipid ratio.

Detailed Description Text (46):
It has been previously described in Biochemistry, 21:3927-3932 (1982) that at concentrations higher than about 1 um, doxorubicin forms dimers and higher molecular weight aggregates. Since the concentration achieved in the ammonium sulfate liposomes far exceeds this limit, the physical state of this drug inside the vesicles was studied. The simplest physical parameter that changes by aggregation is the absorbance spectrum of the drug. The ratio of absorbance at 470 nm to the absorbance at, 550 nm can give a semi-quantitative parameter for the aggregation state of the drug. Table 2 presents data on this ratio for high concentrations of doxorubicin in solution, and also on the same parameter from the doxorubicin loaded liposomes. Measurements were carried out on a Perkin Elmer Lambda 3B dual beam spectrophotometer. The ratio in liposomes was obtained as a different spectrum in which "empty" liposomes, i.e., not containing doxorubicin were prepared using the same lipid composition and in identical way served as a control. By using this procedure the light scattering of the liposomes was corrected. In both cases a substantial aggregation of the drug can be inferred from the data. Such aggregation however, is in no way detrimental for the release of doxorubicin from the liposomes.

Detailed Description Text (51):
Table 4 and FIG. 4 show data on the leakage rate from the two types of liposomes. FIG. 4 illustrates leakage of doxorubicin from liposomes. The figure compares leakage from liposomes with either membrane associated or aqueous phase entrapped

doxorubicin. The latter were prepared by the ammonium sulfate loading method as described in the examples using DPPC/cholesterol (-.-.-.-) and EPC/cholesterol (- - -) liposomes. The membrane associated type of liposomes where composed of EPC/EPG/cholesterol in ratio of (7/3/4;mol/mol/mol) containing traces of .sup.3 H-cholestearyllinoleate.

Detailed Description Text (73):
Effect of liposome type on ammonium gradient dependent loading of doxorubicin. Table 5 shows a comparison of doxorubicin loading into three types of multilamellar (Avanti) EPC/cholesterol liposomes as a result of ammonium ion gradient. In all cases the gradient was obtained by gel exclusion chromatography of the liposomes after ammonium sulfate loading. The incorporated doxorubicin was removed by Dowex after 24 hours incubation at room temperature, and the mole ratio of doxorubicin to phospholipids (DXR/PL) was determined. Table 5 demonstrates that loading efficiency is in the order SPLV>FTMLV>MLV. This order is related to the trapped volume of these three MLV types. It is of interest that the MLV are leakier than the SPLV or the FTMLV, suggesting better annealing of the latter two types of MLV.

Detailed Description Text (74):
Stability of liposomes loaded with doxorubicin was determined by characterization of the physical and chemical stability of egg PC/cholesterol liposomes loaded with doxorubicin by the ammonium sulfate gradient method. The leakage of DXR is temperature dependent with rather high energy of activation. The first stage of the physical stability studies was to follow the change in DXR/phospholipid mole ratio of the MLV prepared by 3 different methods described in Table 5.

Detailed Description Text (118):
Liposomes were prepared as described in Example 3A using fresh 95% EPC/cholesterol in 2:1 molar ratio. pH gradient was formed by removal of external ammonium sulfate by gel exclusion chromatography as described Examples 1A, 2A, 3A. Half of the liposomes was used for loading of doxorubicin using this method. Other half was injected into tail veins of 6 BALB-C mice at the level of 350 mg PC per kg. The mice were followed for 6 months. None of the mice died and all of them behaved normally. At this level the ammonium sulfate liposomes were non-toxic.

Detailed Description Text (121):
Ammonium sulfate liposomes were prepared exactly as in Example 2A above. After separation of untrapped ammonium sulfate by Sephadex G- 50, 1 ml of the liposome dispersion was mixed with 10 mg of daunorubicin dissolved in 1 ml of 50.degree. C. and at specified time intervals aliquots were taken. Free daunorubicin was removed by the same Dowex method described for doxorubicin in Examples 1A, 2A, 3A, and the daunorubicin concentration was measured as shown for doxorubicin. It was found that the loading was finished in I hour, and the final molar ratio of daunorubicin to phospholipid achieved was 1:6.

Previous Doc Next Doc Go to Doc#

Refine Search

Search Results -

Terms	Documents
L2 and (ammonium adj1 sulfate)	0

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L3

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Monday, March 19, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L3	L2 and (ammonium adj1 sulfate)	0	L3
L2	(preliposome or proliposome) same (ethanol or alcohol)	15	L2
L1	liposome same (ethanol or alcohol) same (ammonium adj1 sulfate)	28	L1

END OF SEARCH HISTORY

L1: Entry 23 of 28 File: USPT Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355268 B1
** See image for Certificate of Correction **
TITLE: Liposome-entrapped topoisomerase inhibitors

Detailed Description Text (112):
The dissolved lipid solution was transferred to another 250 mL round bottom flask containing 100 mL of 250 mM ammonium sulfate solution equilibrated to 65.degree. C. The ethanol:lipid:ammonium sulfate hydration mixture was mixed continuously for at least one hour while maintaining the temperature using a 65.degree. C. water bath to form oligolamellar ethanol hydration liposomes.

Detailed Description Text (116):
Ammonium sulfate and ethanol were removed from the external bulk aqueous phase immediately prior to remote loading by hollow fiber tangential flow diafiltration with a 100 kDa nominal molecular weight cutoff cartridge. Constant feed volume was maintained, and at least seven exchange volumes were used resulting in liposomes suspended in an exterior aqueous phase comprised of 10% sucrose.

L1: Entry 24 of 28 File: USPT Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051251 A
TITLE: Liposome loading method using a boronic acid compound

Detailed Description Text (53):
The liposome suspension was prepared by dissolving the lipids in ethanol and drying the lipids to a thin film. The lipid film was hydrated with an ammonium sulfate solution to form liposomes and then the liposomes were extruded to obtain liposomes of about 100 nm. The liposome suspension was dialyzed against a sucrose solution, thus obtaining liposomes encapsulating a 250 mM ammonium sulfate solution in an external buffer of 10% sucrose at pH 6.5. The total lipid concentration was 52 .mu.moles/ml.